Amendments to the Claims

Claim 1 (currently amended): A method of detecting and ~~analysing~~analyzing differences between nucleic acids from two sources, which method comprises:

a. providing the nucleic acids from two sources as ~~labelled~~labeled probes wherein the nucleic acids from two sources are ~~labelled~~labeled with two different markers;

b. forming a mixture of the ~~labelled~~labeled probes with pooled reagents wherein each of the pooled reagents comprises a population of beads carrying a polynucleotide target, the polynucleotide target of any one of the pooled reagents being different from the target of any other of the pooled reagents and the beads of any one of the pooled reagents being distinguishable from the beads of any other of the pooled reagents;

c. incubating the mixture under conditions to promote specific ~~hybridisation~~hybridization between probes and targets; and

d. ~~analysing~~analyzing beads in the mixture by flow cytometry.

Claim 2 (original): The method of claim 1 wherein the nucleic acids from two sources are mRNA or cDNA from cells or tissues.

Claim 3 (previously amended): The method of claim 1 wherein the polynucleotide targets are cDNA derived from cellular mRNA.

Claim 4 (previously amended): The method of claim 1 wherein the polynucleotide targets

are PCR amplimers.

Claim 5 (previously amended): The method of claim 1 wherein the polynucleotide targets contain terminal biotin groups through which they are attached to streptavidin-coated beads.

Claim 6 (previously amended): The method of claim 1 wherein the polynucleotide targets are single-stranded nucleic acids.

Claim 7 (previously amended): The method of claim 1 wherein the nucleic acids are single-stranded nucleic acids.

Claim 8 (previously amended): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by size.

Claim 9 (previously amended): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the nature of one or more markers attached to the beads.

Claim 10 (previously amended): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the concentration of one or more markers attached to the beads.

Claim 11 (previously amended): The method of claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the size and/or by the nature and the concentration of one or more markers attached to the beads.

Claim 12 (previously amended): The method of claim 9 wherein the markers are fluorescent markers attached to the beads.

Claim 13 (previously amended): The method of claim1 wherein each of the nucleic acids is labelled with a fluorescent tag to indicate its source.

Claim 14 (previously amended): The method of claim 1 wherein the analysis by flow cytometry is performed to identify each bead and to quantify the probes bound thereto.

Claim 15 (previously amended): The method of claim 1 further comprising the step of analysing the data obtained by flow cytometry to yield information about the relative and/or absolute abundances of individual nucleic acid sequences contained within the nucleic acids from two sources.

Claim 16 (previously added): The method of claim 10 wherein the markers are fluorescent markers attached to the beads.

Claim 17 (previously added): The method of claim 11 wherein the markers are fluorescent markers attached to the beads.

Remarks

Claims 1-17 are pending in the captioned application. Applicants have amended claim 1 to correct typographical errors at the Examiner's request. Additionally, Applicants have amended claim1, lines 3, 4, and 5 to correct additional typographical errors. Applicants respectfully assert that all amendments are properly based on the specification and earnestly request their entry.

The Examiner has rejected claims 1-17 under U.S.C. 102(a) as "being anticipated by Kamb et al. (PCT international application Number WO 98/26098) (June 18, 1998)." The Examiner states: "Kamb et al. teaches a method of detecting and analyzing differences between nucleic acids from two sources (Abstract), which method comprises: a. providing the nucleic acids from two sources as labeled probes...; b. forming a mixture of the labeled probes with pooled reagents...; c. incubating the mixture...; and d. analyzing each bead in the mixture by flow cytometry". Applicants respectfully traverse this rejection.

Applicants respectfully point out to the Examiner the differences between the current invention and the Kamb invention. In the method of the present invention, "each of the pooled reagents comprises a population of beads carrying a polynucleotide target, the polynucleotide target of any one of the pooled reagents being different from the target of any other of the pooled reagents", and "the beads of any one of the pooled reagents being distinguishable from the beads of any other of the pooled reagents" by flow cytometry (claim 1b, Figure 2, Figure 4). In other words, each bead of a detectable type carries the same known nucleic acid sequence. Incubation of the beads with a mixture of

differently labeled probes from two sources, and subsequent analysis of the beads in the mixture by flow cytometry, allows direct quantification of the relative abundance of any specific, known target.

Kamb et al. discloses a method for determining the identity of unknown sequences that are differentially expressed in two samples. In the Kamb method, each of the solid support (bead) has "attached thereto multiple oligonucleotides or nucleic acid fragments of a unique sequence" (claim 1(b)). However, beads carrying one unique sequence are NOT distinguishable from beads carrying a different unique sequence, by flow cytometry, and the identity of the unique sequence can not be determined during flow sorting. In fact, an additional step has to be taken to determine "the identity of nucleic acid molecules' of interest (claim 1 (d)).

In view of the foregoing, Applicant submit that claims 1-17 cannot by anticipated by Kamb et al. Applicant respectfully requests that the above rejection be withdrawn.

Early and favorable action is earnestly solicited.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on July 18, 2003.

Signature:

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